Program/Abstract # 473
Examination of the roles of Nkx2.1 and Fgf10 in *Xenopus laevis* lung development
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We are interested in examining the viability of *Xenopus laevis* as a model organism in which to study the earliest events of lung development. Previously we sequenced and characterized the expression of the lung specific genes Surfactant protein C (Spc) and Surfactant protein B (Spb). These genes are exclusively expressed in the embryonic and adult lung and share significant homology with their mammalian homologs. Here we report the sequence of xFgf10, the *Xenopus* homolog to the mouse Fgf10 gene necessary for lung development. In addition, we report the effect of overexpressing the transcription factor Nkx2.1 in endodermal cells fated to form lung. Nkx2.1 is expressed at the earliest stages of lung development in mice and frogs, is necessary for proper lung formation in mice and is necessary for the expression of the lung specific genes Spc and Spb in cultured mouse cells. Overexpression of *Xenopus* Nkx2.1 resulted in increased expression of Spc as measured by real-time PCR. The effect of Nkx2.1 on Spb expression is currently being examined.

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Program/Abstract # 474
Ngn3 expression in differentiated islet cells contributes to islet cell maintenance and function
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It is well-established that Ngn3 is both necessary and sufficient to induce endocrine islet cell differentiation during embryogenesis. Because detectable Ngn3 is only detectable in progenitor cells that will eventually become hormone-expressing islet cells, but not in hormone-positive cells, it has been proposed as an endocrine progenitor cell marker. Here we present several pieces of evidence to suggest the presence of sustained Ngn3 expression and its functional involvement in the adult islet cells. (1), our RT-PCR and western blot-based studies show that Ngn3 mRNA and protein are present in wild type adult islet cells and this expression is enhanced by partial pancreatectomy. (2), immunofluorescence reveals the presence of discrete nuclear Ngn3 signals in differentiated islet cells at several stages. (3), a Ngn3-CreERT knockin mouse specifically activate Cre reporter in adult islet cells. (4), Ngn3 inactivation specifically in differentiated islet cells compromises endocrine function. Finally, inactivation of Ngn3 in post-differentiated islet cells compromise the expression of several genes that are known to be regulated by Ngn3 at embryonic stages. Specifically loss of Ngn3 function in islet cells reduced the expression of Glut2, MafA, Nkx6.1, and Pdx1, but not insulin and MafB. These findings suggest that Ngn3 expression exist in the adult islet cells and this expression contributes to endocrine functional maintenance.

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Program/Abstract # 475
Myt1 and Ngn3 form a feed-forward expression loop to promote endocrine islet cell differentiation
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High levels of Ngn3 expression in pancreatic progenitor cells are both necessary and sufficient to initiate endocrine differentiation. While it is clear that the Notch-Hes1-mediated signals control the number of Ngn3-expressing cells in the developing pancreas, it is not known what factors control the level of Ngn3 expression in individual pancreatic cells. Here we report that Myt1b and Ngn3 form a feed-forward expression loop that regulates endocrine differentiation. Myt1b induces glucagon expression by potentiating Ngn3 transcription in pancreatic progenitors. Vice versa, Ngn3 protein production induces the expression of Myt1. Furthermore, pancreatic Myt1 expression largely, but not totally, relies on Ngn3 activity. Surprisingly, a portion of Myt1 expressing pancreatic cells express glucagon and other α cell markers in Ngn3 nullizygous mutant animals. These results demonstrate that Myt1b and Ngn3 positively regulate each other's expression to promote endocrine differentiation. In addition, the data uncover an unexpected Ngn3 expression-independent endocrine cell production pathway, which further bolsters the notion that the seemingly equivalent endocrine cells of each type, as judged by hormone and transcription factor expression, are heterogeneous in their origin.

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Program/Abstract # 476
Thyroid hormone controls remodeling of the exocrine and endocrine pancreas during metamorphosis in *Xenopus laevis*
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At metamorphosis the *Xenopus laevis* tadpole exocrine pancreas remodels in two stages. At climax thyroid hormone (TH) induces dedifferentiation of the entire exocrine pancreas to a progenitor state. The mRNAs that encode exocrine specific proteins undergo almost complete extinction at climax while PDX-1, Notch-1 and Hes-1, genes implicated in differentiation of the progenitor cells, are activated. At the end of spontaneous metamorphosis the pancreas begins to redifferentiate. A major difference between a tadpole and frog pancreas is the paucity of ducts in the tadpole. The redifferentiated frog pancreas has typical ducts found in other vertebrate pancreases. Exogenous TH induces the dedifferentiation phase not the redifferentation phase. Pancreases of transgenic tadpoles expressing a dominant negative form of the thyroid hormone receptor (TRDN) controlled by the elastase promoter are resistant to TH. Their acinar cells do not down regulate exocrine specific genes or activate Notch-1 and Hes-1. These transgenic frogs do not form a normal ductal system. The dedifferentiation of the exocrine pancreas at climax also controls maturation of the endocrine pancreas by allowing the preexisting beta cell (insulin) to cluster and form islets. Exogenous TH induces the clustering of beta cell and expression of the TRDN transgene or exposure of premetamorphic tadpoles to the anti-thyroid compound, methimazole inhibit the clustering. Therefore, the TH-dependent dedifferentiation of the exocrine pancreas at climax is